APPLICATION OF AN EMPIRICAL APPROACH FOR PREDICTING ACCURACY FOR GENOMIC EVALUATIONS

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SUMMARY

Including genomics in genetic evaluations can effectively increase selection response, especially for hard to measure, sex limited, and late in life traits. Modelling the increase in accuracy is useful when designing reference data projects and when breeders choose animals to genotype. Theoretical equations exist to predict the EBV accuracy of un-phenotyped animals. However, there are anecdotal reports that the accuracy obtained in practice was often lower than theoretical predictions. This paper validated an empirical approach to predicting accuracy in Australian Brahman data for nine traits. The empirical approach required the accuracy of reference and target animals from a standard pedigree BLUP genetic evaluation and the accuracy of reference animals from a GBLUP genetic evaluation. Using this information, a series of equations were applied to obtain the predicted GBLUP accuracy for target animals. Forward cross-validation showed that the empirical predicted GBLUP was comparable to the actual GBLUP accuracy observed for target animals (accuracy differed between 0.9% and 3.6%). In contrast, theoretical predictions differed from the observed GBLUP accuracy between 5.2% and 21.8%. For smaller (<4,000) reference populations, the theoretical accuracy was closer to the observed GBLUP accuracy, with differences ranging from 5.2% to 11.6%. The theoretical accuracy was overestimated by between 20.7% and 21.8% for larger reference populations. Empirical estimates of the effective number of chromosome segments (M_e) were between 2.0 and 3.9 times that of theoretical M_e, with the greatest difference being for the traits with larger reference sizes. This suggests that the theoretical M_e is the reason for overestimated theoretical accuracy predictions.

INTRODUCTION

Selection response is linear with increasing EBV accuracy, and genomic selection can be an effective way of increasing accuracy, especially for hard or expensive to measure traits, late in life, and sex-limited traits. For genomic selection to be effective, reference data with genotyped and phenotyped animals are required, and generally, the larger the reference size, the greater the accuracy (Goddard and Hayes 2009). Constructing reference data to underpin genomic selection can be expensive, especially for traits not commonly recorded by the industry. Therefore, predicting EBV accuracy is useful for designing reference data projects. Accuracy predictions are also useful for breeders deciding which animals to genotype and the value they can expect from their investment. There have been several theoretical predictions formulated to predict EBV accuracy of un-phenotyped animals given different population parameters (Daetwyler *et al*. (2008), Goddard and Hayes (2009), Goddard *et al*. (2011)). However, there have been anecdotal reports that accuracy from national genetic evaluations was often lower than the theoretical predictions. Dekkers *et al*. (2021) proposed an empirical approach for predicting EBV accuracy. This method bases predictions on the accuracy of reference and target animals from pedigree BLUP and GBLUP genetic evaluations. This study aimed to apply Dekkers' empirical approach using an Australian Brahman beef cattle dataset and validate the prediction accuracies for nine traits using forward cross-

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validation.

MATERIALS AND METHODS

Full details of Dekkers' empirical method for estimating the effective number of chromosome segments (M_e) and predicted EBV accuracy are in Dekkers *et al*. (2021). In brief, this approach requires two genetic evaluations to be undertaken. The first is a BLUP evaluation with full pedigree (including target animals) and phenotypes of reference animals. The second was a GBLUP analysis using the phenotypes and genotypes of reference animals. The average BLUP and GBLUP accuracy for reference animals and average BLUP accuracy for target animals, along with population parameters (i.e. reference size, heritability and genome size) were used in a series of equations that iteratively updated M_e until estimates were stable, and predicted GBLUP accuracy for target animals. M_e was estimated with the equation below, where N was the number of reference animals, q_D^2 the proportion of genetic variance captured by the genotypes (initially $q_D^2 = 1$ but was recalculated each iteration using $q_D^2 = \frac{m}{m+M_e}$ where m = number of markers), h^2 the trait heritability and θ_{Dr} the Fisher information statistic of the reference animals. Dekkers' predicted GBLUP accuracy of target animals (r_{Gt}; equation below) was calculated based on the average accuracy of target animals from the BLUP analysis (r_{At}) and the contribution of G above that of A for target animals (r_{Dt}). For target animals, r_{Dt} was a function of the contribution of G above that of A for reference animals (calculated from average BLUP and GBLUP accuracy) and the number of generations between reference and target animals.

$$M_e = \frac{Nq_D^2h^2}{\theta_{Dr}} \qquad r_{Gt} = \sqrt{\frac{r_{At}^2 + r_{Dt}^2 - 2r_{At}^2 r_{Dt}^2}{1 - r_{At}^2 r_{Dt}^2}}$$

Pedigree, pre-adjusted phenotypes and genotypes were obtained from the Brahman BREEDPLAN genetic evaluation. Genotypes were from different commercially available SNP chips, and after imputation and QA as part of the BREEDPLAN evaluation, 67,327 SNPs were available for analysis. Nine traits were considered; four hard to measure traits (shear force, lactation anoestrus interval, percent normal sperm, age of puberty) and five that were widely recorded (ultrasound scanned EMA, scrotal size, 200, 400 and 600-day live weight) in seedstock herds. All traits were recorded following BREEDPLAN protocols.

Forward cross-validation was used to validate Dekkers' empirical method. Reference (genotyped and phenotyped) animals were split based on year of birth, with the earliest animals remaining reference animals and more recent animals considered target animals with phenotypes and genotypes assumed unknown. The birth year that defined reference and target groups varied for each trait, such that approximately 70% of the data was the reference and the remaining 30% target animals. A five-generation pedigree was built for reference and target animals, and three analyses were performed; 1. BLUP evaluation with reference phenotypes and five-generation pedigree, 2. GBLUP evaluation with reference phenotypes and genotypes, and 3. GBLUP evaluation with reference phenotypes and the genotypes of both reference and target animals. Analysis 1 and 2 were used to apply Dekkers' equations to obtain predicted GBLUP accuracy of target animals (r_{Gt}) and population M_e. While analysis 3 was undertaken to get the observed GBLUP accuracy for target animals, which was then compared with Dekkers' predictions. The same set of genetic parameters and models were used for each analysis. For all analyses, WOMBAT was used and exact accuracy based on the models and data obtained (Meyer 2007). Theoretical accuracy was calculated using Daetwyler *et al*. (2008), where $M_e = (2N_eLk)/ln(N_eL)$ from Goddard *et al*. (2011) and compared with Dekkers' prediction and the observed GBLUP accuracy. To theoretically derive M_e, the effective population size of the breed was estimated using RelaX2 (Stranden, 2014) software and was estimated to be 141.6 animals. The size of the chromosomes (L) was 1.017M (Snelling et al. 2007) with 29 autosomal chromosomes (k) represented on the SNP chips.

RESULTS AND DISCUSSION

Table 1 records the number of reference and target animals, assumed trait heritability and average BLUP and GBLUP accuracy (empirical analyses 1 and 2). The number of reference animals ranged between 982 (shear force) and 11,541 (200-day live weight). Average accuracy from the BLUP analysis ranged from 0.47 (shear force) to 0.77 (age at puberty) for reference animals and between 0.19 (percent normal sperm) and 0.39 (600-day live weight) for target animals. BLUP EBVs of target animals were based on pedigree relationships to the phenotyped reference animals. Reference animals had BLUP accuracies between 0.22 (ultrasound EMA) and 0.42 (age at puberty) higher than target animals. An additional but smaller increase in accuracy was observed for reference animals when genotypes were included in a GBLUP analysis; increases in accuracy ranged between 0.02 (lactation anoestrus interval) and 0.11 (200-day live weight).

Table 1. Number of reference and target animals, assumed heritability and average accuracy from BLUP and GBLUP analysis of Brahman reference (REF) and target (TAR) animals

Trait	Number of animals		h^2	Average accuracy		
	REF	TAR		BLUP REF	GBLUP REF	BLUP TAR
Shear force (kg)	982	511	0.26	0.47	0.50	0.21
Lactation anoestrus interval (days)	1,048	470	0.40	0.68	0.70	0.30
Percent normal sperm (%)	1,366	583	0.25	0.52	0.55	0.19
Age of puberty (day)	1,670	806	0.57	0.77	0.80	0.35
Heifer ultrasound scanned EMA (cm^2)	2,565	1,393	0.21	0.52	0.57	0.30
Scrotal size (cm)	4,351	1,988	0.48	0.67	0.73	0.32
600-day live weight (kg)	7,805	3,673	0.51	0.70	0.78	0.39
400-day live weight (kg)	8,730	4,832	0.41	0.67	0.75	0.37
200-day live weight (kg)	11,541	4,415	0.25	0.59	0.70	0.36

Table 2. The estimated effective number of chromosome segments (M_e) and predicted accuracy from Dekkers' empirical approach (Prediction), the GBLUP accuracy from forward cross-validation (observed) and the Daetwyler theoretical prediction (Theoretical)

Trait	M_e	Accuracy of target animals		
		Prediction	Observed	Theoretical[1]
Shear force (kg)	4,500.64	0.29	0.28	0.36
Lactation anoestrus interval (days)	3,425.78	0.42	0.40	0.45
Percent normal sperm (%)	4,252.34	0.32	0.30	0.41
Age of puberty (day)	3,997.45	0.52	0.49	0.60
Ultrasound scanned EMA (cm^2)	4,640.22	0.41	0.40	0.49
Scrotal size (cm)	5,740.04	0.56	0.53	0.74
600-day live weight (kg)	6,550.21	0.63	0.61	0.84
400-day live weight (kg)	6,359.78	0.66	0.63	0.83
200-day live weight (kg)	6,227.21	0.60	0.58	0.80

[1] theoretical prediction based on Daetwyler *et al.* (2008) method where M_e = 1,680.23 (N_e = 141.6)

The predicted accuracy from Dekkers' empirical (Prediction) and Daetwyler's theoretical (Theoretical) method are shown in Table 2, along with the observed GBLUP accuracy (Observed) of target animals. The difference between Dekkers' empirical and Daetwyler's theoretical accuracy was smaller (0.03 to 0.09) with smaller reference sizes, and Dekkers' empirical prediction was lower than Daetwyler's theoretical prediction. However, for traits with more than 4,000 reference animals, the difference between Dekkers' empirical and Daetwyler's theoretical predictions was much larger

(0.12 to 0.15). The observed GBLUP accuracy of target animals (analysis 3) showed that Dekkers' empirical predictions were closer to the observed accuracy than Daetwyler's theoretical accuracy. The observed accuracy was slightly lower (0.01 to 0.04) than Dekkers' empirical predictions. The comparison with Daetwyler's theoretical accuracy showed larger differences. For traits with fewer than 4,000 animals in the reference, theoretical accuracies were between 0.05 and 0.12 higher than the observed accuracy. The differences for traits with larger reference sizes ranged between 0.21 and 0.22. These differences can be explained by the theoretical M_e term being underestimated. Table 2 shows the empirically estimated M_e with estimates varying for each trait; for all traits empirical M_e was much larger than theoretical M_e. Empirical M_e increased with increasing reference size, suggesting a greater diversity of DNA represented in larger references. For traits with smaller references, empirical M_e was 2.0 to 2.8 times larger than theoretical M_e, and for traits with larger reference sizes, empirical M_e was 3.4 to 3.9 times larger. The theoretical M_e was a function of the effective population size and was constant across all traits.

These results demonstrate that Dekkers' empirical approach effectively predicted EBV accuracy, especially for larger reference sizes where theoretical methods overestimate accuracy. It was observed (results not shown) that spurious results occurred for the empirical method when the reference size was small (less than ~1,000 animals). However, with small reference sizes, genomic selection will have limited benefits over pedigree-based selection. The empirical method is only suitable once reference datasets with more than 1,000 animals exist, which limits its application for project design or breeds not yet undertaking genomic selection. It may be possible to use estimates from other breeds and traits to predict accuracy in these situations, but further work is needed to confirm this. One advantage of Dekkers' empirical method is the ability to make predictions for different subsets of target animals. This validation study obtained the BLUP accuracy for target animals from a pedigree BLUP analysis. However, an alternative may be to use an assumed accuracy for target animals. Therefore, predictions can be made for a range of scenarios, including "cleanskins" where no pedigree or phenotypes are available (i.e. BLUP accuracy=0), animals that are not phenotyped but have phenotyped relatives and already phenotyped animals (i.e. BLUP accuracy will be higher than for un-phenotyped animals). In contrast, current theoretical predictions apply to one scenario, assuming that the target animals are un-phenotyped but have pedigree recorded and do not consider other scenarios.

CONCLUSIONS

Predicting the accuracy that can be achieved from genomic selection is desirable. This paper demonstrated that an empirical approach for accuracy prediction was effective and provided better predictions than existing theoretical approaches. However, the method does rely on reference datasets being available.

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